"UCLA SPORE IN LUNG CANCER - Core 1: Clinical "A Phase I/II Trial Evaluating Intratumoral Injection of Interleukin-7 Gene Modified Autologous Dendritic Cells for the Treatment of Non-Small Cell Lung Cancer,"

Scientific Abstract

Lung cancer is the leading cause of cancer-related death in the United States. Because overall 5-year survival is less than 15%, entirely new therapeutic strategies are needed. We now have a clearer understanding of the problem: while lung cancers express tumor antigens, they are ineffective as antigen presenting cells. In fact, the tumor's lack of costimulatory molecules, in combination with the tumor's production of inhibitory peptides, promotes a state of specific T cell anergy . In this proposal we will evaluate a new approach for using DC (dendritic cells) to treat lung cancer. We have developed a murine model in which bone marrow-derived, ex vivo activated DC are genetically modified to secrete IL-7 and utilized to treat established lung cancer via intratumoral administration. We hypothesize that intratumoral injection of autologous dendritic cells (DC), modified by infection with a replication-deficient adenoviral (AdV) vector expressing the interleukin-7 (IL-7) gene, will take-up and process tumor-derived antigens from the local environment, traffic to regional lymph nodes, and stimulate effective anti-tumor immunity. The overall goal of the studies in this proposal will be to determine the immunologic mechanisms responsible for DC-AdIL-7-mediated tumor eradication. Our specific objectives are: 1) To determine the safety and maximal tolerated dose (MTD) of IL-7 gene-modified DC (AdV-IL-7-DC) when administered as an intratumoral injection into the primary tumor site of patients with advanced non-small cell lung cancer (NSCLC). 2) To determine the local and systemic biologic activity (i.e. generation of anti-tumor immunity) of AdV-IL-7-DC when administered intratumorally at the MTD to patients with advanced NSCLC. 3) To determine the clinical activity (i.e. reduction in tumor burden) of AdV-IL-7-DC when administered intratumorally at the MTD to patients with advanced NSCLC.